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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/670,096	09/26/2000	Linda S. Mansfield	MSU 4.1-526	7494

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/670,096	MANSFIELD ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In accordance with Board's the decision, dated on 5/25/06, the examiner is reopening the prosecution to consider the patentability of instant claims of record. Therefore, the finality of office action mailed on 2/23/04 is withdrawn.

Status of the Claims

2. Claims 1, 2 and 21 are pending.

Claim Rejections - 35 USC 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) Liang et al 1997 (Analytical Biochemistry; 250 (1) 61-5) or each in view of Harlow and Lane 1988 (IDS: Antibodies; especially chapter 5 and 6 Cold Spring Harbor).

Claim 1 is directed to a composition for treating an equid infected with Sarcocystis neurona comprising a mixture of isolated antibodies against 16 kDa antigen of Sarcocystis neurona and isolated antibodies against a 20kDa antigen of Sarcocystis neurona wherein the antibodies are from serum of an animal immunized with the antigen and wherein the mixture is in a pharmaceutically acceptable carrier.

Examiner interprets antibodies as monoclonal or polyclonal antibodies

Liang et al 1998 identified four major immunoblot patterns based on the analysis of 25,000 equine serum and cerebrospinal fluid (CSF) samples, including samples from horses with neurological signs typical of equine myeloencephalitis (EPM) or with histologically or parasitologically confirmed EPM (see Materials and Methods, pages 1834-1835) using *S.neurona* merozoite antigens. The four immunoblot patterns based on the combinations of Sn 30, 16, 14 and 11 (30KD, 16KD, 14KD and 11KD respectively) proteins are represented in Figure 1. As shown in Figure 3, the intensity of 30KD, 16KD, and 14KD antigens was greatly reduced after treatment with trypsin indicating that these proteins are surface proteins of merozoites and were accessible to the action of enzyme. The prior art identified 30KD and 16KD antigens as cell surface antigens of merozoites. A combination of the results of western-blot analysis (figure 1) and trypsin digestion (figure 3 B) suggests that these are important surface proteins that could be used in specific diagnosis of S.neurona infection, as candidate antigens for vaccine development and specific antibodies to these antigens lyse merozoites via complement or inhibit their attachment and penetration to host cells (see abstract, figure 1& figure 3 B). Further, the prior art suggests that monoclonal antibodies are often used to study parasitic proteins and combination of techniques including western-blot analysis (figure 1) and trypsin digestion has been shown to be effective in the identification of specific surface antigens (page 1837, right column, first and second paragraphs). *S.neurona* infection in horses induced

antibodies to 16 KD and 30 KD antigens indicating that these proteins are strong immunogens. Antibodies to 16KD antigen not only recognized the 16KD antigen but also lysed the merozoites in *in vitro* neutralization assays (see Discussion and page 1836, results summarized in group 4). However, antibodies to 30KD recognized the 30KD antigen but could not inhibit *in vitro* neutralization of merozoites, as 30KD antigen appears to cross-react with serum obtained from horses infected with other Sarcocystis species. Thus the prior art teaches 30KD, 16KD, 14KD and 11KD proteins as merozoite surface antigens that are involved in *S.neurona* infection and antibodies to these antigens appear to neutralize parasite merozoites and warrants further investigation as candidate antigens for inclusion in vaccines against S.neurona infection (see 1837, right column, last paragraph).

Liang et al 1997 (see page 65, left column, last paragraph) teach purified 30 KD and 19 KD (i.e. 16KD $_{+/-4}$) antigens from *S.neurona* merozoites by using infected horse serum. Further, the prior art teaches high-resolution purification of these proteins by a combination of SDS-PAGE, isoelectric focusing and membrane blotting (see figure 3). However, the prior art Liang 1998 or Liang 1997 does not teach a composition comprising a mixture of isolated antibodies against 16 kDa antigen of *Sarcocystis neurona* and isolated antibodies against a 30kDa antigen of Sarcocystis neurona. Harlow and Lane teach monoclonal antibodies and polyclonal antibodies to any antigen and using such composition for many immunological purposes.

It would have been prima facie obvious to one, having ordinary skill the art at the time the invention was made to make either monoclonal or polyclonal antibodies to merozoite surface antigens including 16KD and 30KD because Liang et al taught detection of S. neurona infection using serum and sometimes infected horse serum cross reacts with antigens such as 30KD. Further, the art suggests monoclonal antibodies are often used to study parasite (page

1837, last paragraph) proteins and EPM disease occurs after merozoite passes through the vascular endothelium of blood – brain barrier into the central nervous system, and so humoral responses play essential role in blocking this migration and specific cytotoxic T cells are ineffective in attacking merozoite migration to the central nervous system in the blood stream (page 1837, left column, third paragraph). Therefore, an artisan of ordinary skill would have been motivated to use readily available and purified surface antigens (Liang et al 1997) from merozoites including 16KD and 30 KD as disclosed by the prior art Liang et al 1998 or Liang et al 1997 with a reasonable expectation of success for raising antibodies (monoclonal/ polyclonal antibodies) by using well established immunization procedures (chapter 5) and hybridoma technology (chapter 6) as taught by Harlow and Lane 1986 because Liang et al 1998 suggests that humoral immunity to *S.neurona* infection is important (see page 1836 under discussion) in clearing S.neurona merozoites . The art also suggests surface antigens including 30KD, 16KD, 14KD are immunoreactive with infected serum that are useful for the detection of the pathogenic S.neurona and Liang et al 1997 teach purification of target merozoite surface proteins 19 KD, 30 KD and 100KD. Moreover, it has become routine in the art to produce antibodies (monoclonal/ polyclonal antibodies) for characterizing and purifying proteins especially target proteins such as surface proteins of parasites or envelope proteins of bacteria. The claimed invention is prima facie obvious over Liang et al 1998 or Liang et al 1997 and each in view of Harlow and Lane 1986 (chapters 5 and 6) absent any convincing evidence to the contrary.

5. Claims 21 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) and Liang et al 1997 (Analytical Biochemistry; 250 (1) 61-5) each in view of Harlow and Lane 1988 (IDS: Antibodies; especially chapter 5 and 6 Cold Spring Harbor).

Claims are drawn to a method for treating an equid infected with *S.neurona* comprising: (a) providing a mixture of antibodies against a 16 kD antigen and a 30 kD antigen, both of which are specific to *S. neurona*, wherein the antibodies are selected from the group consisting of polyclonal antibodies from serum from an animal immunized with the antigen and monoclonal antibodies from a hybridoma, and wherein the antibodies are in a pharmaceutically acceptable Liang et al 1998 teach a method of inhibiting merozoite activity (page 1835, right column, second para through 1836, left column) comprising providing a mixture of antibodies obtained from 25,000 equine serum and cerebrospinal fluid (CSF) samples and identified four band patterns. The four-immunoblot patterns based on the combinations of Sn 30, 16, 14 and 11 (30KD, 16KD, 14KD and 11KD respectively) proteins are represented in Figure 1. As shown in Figure 3, the intensity of 30KD, 16KD, and 14KD antigens was greatly reduced after treatment with trypsin indicating that these proteins are surface proteins of merozoites and were accessible to the action of enzyme. The prior art identified 30KD and 16KD antigens as cell surface antigens of merozoites. A combination of the results of western-blot analysis (figure 1) and trypsin digestion (figure 3 B) suggests that these are important surface proteins that could be used in specific diagnosis of S.neurona infection, as candidate antigens for vaccine development and specific antibodies to these antigens lyse merozoites via complement or inhibit their attachment and penetration to host cells (see abstract, figure 1& figure 3 B). Further, the prior art suggests that monoclonal antibodies are often used to study parasitic proteins and combination of techniques including western-blot analysis (figure 1) and trypsin digestion has been shown to be effective in the identification of specific surface antigens (page 1837, right column, first and second paragraphs). *S.neurona* infection in horses induced antibodies to 16 KD and 30 KD antigens indicating that these proteins are strong immunogens. Antibodies to 16KD antigen not only recognized the 16KD antigen but also lysed the merozoites

in *vitro* neutralization assays (see Discussion and page 1836, results summarized in group 4). However, antibodies to 30KD recognized the 30KD antigen but could not inhibit *in vitro* neutralization of merozoites, as 30KD antigen appears to cross-react with serum obtained from horses infected with other Sarcocystis species. Thus the prior art teaches a method of inhibiting merozoite (neutralize parasite merozoites) using a mixture of antibodies to surface antigens 16, 14 and 11 KD etc and warrants further investigation as candidate antigens for inclusion in vaccines against *S.neurona* infection (see 1837, right column, last paragraph).

Liang et al 1997 (see page 65, left column, last paragraph) teach purified 30 KD and 19 KD (i.e. 16KD $_{+/-4}$) antigens from *S.neurona* merozoites by using infected horse serum. Further, the prior art teaches high-resolution purification of these proteins by a combination of SDS-PAGE, isoelectric focusing and membrane blotting (see figure 3). However, the prior art Liang 1998 or Liang 1997 does not teach a composition comprising a mixture of monoclonal antibodies. Harlow and Lane teach monoclonal antibodies and polyclonal antibodies (see chapter 5 and 6) by immunizing animals against a given antigen, preparing hybridoma to obtained monoclonal antibodies, useful for various immunological purposes.

It would have been prima facie obvious to one, having ordinary skill the art at the time the invention was made to make either monoclonal or polyclonal antibodies to merozoite surface antigens including 16KD and 30KD because Liang et al taught antibodies to surface antigen can inhibit infection in neutralization assays. Further, the art suggests monoclonal antibodies are often used to study parasite (page 1837, last paragraph) proteins and humoral responses play essential role in blocking this migration and specific cytotoxic T cells are ineffective in attacking merozoite migration to the central nervous system in the blood stream (page 1837, left column, third paragraph). Therefore, an artisan of ordinary skill would have been motivated to use readily available and purified surface antigens (Liang et al 1997) from

merozoites including 16KD and 30 KD as disclosed by the prior art Liang et al 1998 or Liang et al 1997 with a reasonable expectation of success for raising antibodies (monoclonal/ polyclonal antibodies) by using well established immunization procedures (chapter 5), hybridoma technology (chapter 6) as taught by Harlow and Lane 1986 and using polyclonal (mixture of antibodies) or mixture of monoclonal antibodies in a method of for inhibiting infection in an equid infected with *S.neurona* infection by inoculating mixture of antibodies because Liang et al 1998 suggests that humoral immunity to *S.neurona* infection is important (see page 1836 under discussion) in clearing *S.neurona* merozoites in an invitro method (neutralization) Further, the art clearly suggests that not all antibodies generated during infection will neutralize the merozoites and extended exposure to antiserum (see Liang et al 1998, page 1837, 2nd paragraph, left column in particular) indicating the importance of providing/inoculating infected horses with antibodies. The claimed invention is prima facie obvious over Liang et al 1998 or Liang et al 1997 and each in view of Harlow and Lane 1986 (chapters 5 and 6) absent any convincing evidence to the contrary.

Remarks

6. Claims 1, 21 and 2 are rejected.

Conclusion

7. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published n the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

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